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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,099	07/14/2003	Rebekka M. Wachter	026069-151480US	8511
20350 7590 10/22/2007 TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER EIGHTH FLOOR SAN FRANCISCO, CA 94111-3834			EXAMINER NASHED, NASHAAT T	
			ART UNIT 1656	PAPER NUMBER
			MAIL DATE 10/22/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

**Application No.**

10/620,099

**Applicant(s)**

WACHTER ET AL.

**Examiner**

Nashaat T. Nashed, Ph. D.

**Art Unit**

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10 September 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 143-146, 148-153 and 188-193 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 143-146, 148-153 and 188-193 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Sequence listing error report</u> .    |

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The application has been amended as requested in the communication filed September 10, 2007. Accordingly, claims 143, 144, and 188-190 have been amended and new claims 191-193 have been entered.

Claims 143-146, 148-153, and 188-193 are pending and under consideration.

The sequence listing in a computer readable form (CRF) filed September 10, 2007 is not accepted because of the errors noted on the attached error report. A new CRF containing all the correction cited in the error report is required for reasons of record.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 143-146, 148-153, and 188-193 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 29-37 of U.S. Patent No. 6,150,176 ('176) for the reasons set forth in the prior Office action, mailed May 25, 2005.

Claims 143-146, 148-153, and 188-193 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 4 of U.S. Patent No. 6,780,975 ('975) for the reasons set forth in the prior Office action, mailed May 25, 2005.

In response to the above rejections, applicants requested to held he rejection in abeyance until the claims are found allowable over the prior art.

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The rejection will remain on the record until applicants file a terminal disclaimer. New claims 191-193 are included in these rejections because they are directed to the same subject matter.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 143-146, 148-153, 188, 189, 191, and 193 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the reasons set forth in the prior Office action mailed 3/6/07.

In response to the above rejection, applicants reviewed the Wands factor (Forman factor) separately.

Applicants' arguments filed September 10, 2007 have been fully considered, but they are found unpersuasive. The claim reads on any fluorescent protein having 85% or 90% sequence homology to SEQ ID NO: 2. Enablement requires a disclosure sufficient to allow a person of skill in the art to practice the full scope of the claimed invention without undue experimentation. The previous Office action sets out a *prima facie* case of non-enablement, explaining by sound scientific reasoning why a person of ordinary skill in the art would doubt that the guidance of the specification would enable practice of the full scope of the claimed invention without undue experimentation. Applicants have presented no evidence or, indeed, any arguments to establish the adequacy of the disclosure to enable the scope of the instant claims. Applicants merely assert that the claims are enabled and one of ordinary skill in the art can make mutants. Applicants make no effort to explain why they consider the disclosure of mutants comprising the mutation of handful amino acid residues is sufficient enablement for mutants comprising changing 15% (36 residues) or 10% (24 residues) of the amino acid residues of SEQ ID NO: 2, or any natural fluorescent protein variant of SEQ ID NO: 2 having 85% or 90% sequence homology. Conclusory statements unsupported by evidence or scientific reasoning are insufficient to overcome the *prima facie* case of non-enablement set out in the previous Office action.

The claims are free of prior art.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

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§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTWTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen K. Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nashed/  
Nashaat T. Nashed, Ph. D.  
Primary Examiner  
Art Unit 1656

=====

Sequence Listing could not be accepted due to errors.

See attached Validation Report.

If you need help call the Patent Electronic Business Center at (866)  
217-9197 (toll free).

Reviewer: Anne Corrigan

Timestamp: Thu Oct 11 14:24:59 EDT 2007

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\*\*\*\*\*

Reviewer Comments:

<210> 3

<211> 720

<212> DNA

<213> Artificial sequence

<220>

<223> Engineered Aequorea-related fluorescent protein

<400> 3

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60

ggcgacgtaa acggccacaa gttcagcgtg tccggcgagg gcgagggcga tgccacctac

The above <223> response mentions a protein; however, this is not a  
protein sequence.

<210> 6

<211> 162

<212> TYPE: PRT

<213> Artificial sequence

<220>

<223> Fragment of engineered Aequorea-related fluorescent protein

S65T, positions 68 to 229

<400> 6

Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe

1

5

10

15

Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe

Please remove the "TYPE:" heading in the above <212> response. Do not  
show any alphabetical headings. Also, the top amino acid line is not  
properly aligned with its amino acid numbers.

<210> 23  
<211> 37  
<212> PRT  
<213> Artificial sequence  
<220>  
<223> His-tag amino acid sequence  
<400> 23

Please provide more information in the <223> response above; please give the source of the genetic material.

\*\*\*\*\*

Application No: 10620099

Version No: 2.0

Input Set:

Output Set:

Started: 2007-09-20 14:58:58.525

Finished: 2007-09-20 14:59:00.108

Elapsed: 0 hr(s) 0 min(s) 1 sec(s) 583 ms

Total Warnings: 21

Total Errors: 8

No. of SeqIDs Defined: 23

Actual SeqID Count: 23

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W 213	Artificial or Unknown found in <213> in SEQ ID (4)
W 213	Artificial or Unknown found in <213> in SEQ ID (5)
E 310	Invalid sequence type in <212> in SEQID: (6)
W 213	Artificial or Unknown found in <213> in SEQ ID (6)
E 323	Invalid/missing amino acid numbering SEQID (6) POS (2)
E 323	Invalid/missing amino acid numbering SEQID (6)at Protein (5)
E 323	Invalid/missing amino acid numbering SEQID (6) POS (6)
E 323	Invalid/missing amino acid numbering SEQID (6)at Protein (10)
E 323	Invalid/missing amino acid numbering SEQID (6) POS (11)
E 323	Invalid/missing amino acid numbering SEQID (6)at Protein (15)
E 323	Invalid/missing amino acid numbering SEQID (6) POS (16)
W 213	Artificial or Unknown found in <213> in SEQ ID (7)
W 213	Artificial or Unknown found in <213> in SEQ ID (8)
W 213	Artificial or Unknown found in <213> in SEQ ID (9)
W 213	Artificial or Unknown found in <213> in SEQ ID (10)
W 213	Artificial or Unknown found in <213> in SEQ ID (11)
W 213	Artificial or Unknown found in <213> in SEQ ID (12)
W 213	Artificial or Unknown found in <213> in SEQ ID (13)
W 213	Artificial or Unknown found in <213> in SEQ ID (14)



**Input Set:**

**Output Set:**

**Started:** 2007-09-20 14:58:58.525

**Finished:** 2007-09-20 14:59:00.108

**Elapsed:** 0 hr(s) 0 min(s) 1 sec(s) 583 ms

**Total Warnings:** 21

**Total Errors:** 8

**No. of SeqIDs Defined:** 23

**Actual SeqID Count:** 23

Error code	Error Description
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W 213	Artificial or Unknown found in <213> in SEQ ID (16)
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W 213	Artificial or Unknown found in <213> in SEQ ID (18)
W 213	Artificial or Unknown found in <213> in SEQ ID (19)
W 213	Artificial or Unknown found in <213> in SEQ ID (20)
W 213	Artificial or Unknown found in <213> in SEQ ID (21)
W 213	Artificial or Unknown found in <213> in SEQ ID (22)
	This error has occurred more than 20 times, will not be displayed

<110> WACHTER, Rebekka M.  
 REMINGTON, S. James  
 <120> LONG WAVELENGTH ENGINEERED FLUORESCENT PROTEINS  
 <130> 026069-151480

<140> 10620099  
 <141> 2003-07-14  
 <150> US 09/575,847  
 <151> 2000-05-19  
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 <150> US 08/911,825  
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 <150> US 60/024,050  
 <151> 1996-08-16  
 <160> 23  
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 <211> 716  
 <212> DNA  
 <213> Aequorea victoria  
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aaacttacct ttaaatttat ttgcactact ggaaaactac ctgttccatg gccaacactt	180
gtcactactt tctcttatgg tgttcaatgc ttttcaagat acccagatca tatgaaacgg	240
catgactttt tcaagagtgc catgcccga ggttatgtac agcaaagaac tatatttttc	300
aaagatgacg ggaactacaa gacacgtgct gaagtcaagt ttgaagggtga tacccttggt	360
aatagaatcg agttaaagg tattgatttt aaagaagatg gaaacattct tggacataaa	420
ttggaataga actataactc acacaatgta tacatcatgg cagacaaaca aaagaatgga	480
atcaaagtta acttcaaat tagacacaac attgaagatg gaagcgttca actagcagac	540
tattatcaac aaaatactcc aattctcgat ggccctgtcc ttttaccaga caaccattac	600
ctgtccacac aatctgccct ttcgaaagat cccaacgaaa agagagacca catggtcctt	660
cttgagtttg taacagctgc tgggattaca catggcatgg atgaactata caaata	716

<210> 2  
 <211> 238  
 <212> PRT  
 <213> Aequorea victoria  
 <400> 2

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1 5 10 15	
Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu	
20 25 30	
Gly Glu Gly Asp Val Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys	
35 40 45	
Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Phe	
50 55 60	
Ser Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg	
65 70 75 80	
His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Gln Arg	
85 90 95	
Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val	
100 105 110	

Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile  
 115 120 125  
 Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn  
 130 135 140  
 Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly  
 145 150 155 160  
 Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val  
 165 170 175  
 Gln Leu Ala Asp Tyr Tyr Gln Gln Asn Thr Pro Ile Leu Asp Gly Pro  
 180 185 190  
 Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser  
 195 200 205  
 Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val  
 210 215 220  
 Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys  
 225 230 235

<210> 3  
 <211> 720  
 <212> DNA  
 <213> Artificial sequence  
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 <223> Engineered Aequorea-related fluorescent protein  
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 ggcaagctga ccctgaagtt catctgcacc accggcaagc tgcccgtgcc ctggcccacc 180  
 ctctgaccca ccttcggcta cggcgtgcag tgcttcgccc gctaccgccga ccacatgaag 240  
 cagcaggact tcttcaagtc cgccatgccc gaaggctacg tccaggagcg caccatcttc 300  
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 aagctggagt acaactacaa cagccacaac gtctatatca tggccgacaa gcagaagaac 480  
 ggcataaagg tgaacttcaa gatccgccac aacatcgagg acggcagcgt gcagcccgcc 540  
 gaccactacc agcagaacac ccccatcggc gacggccccg tgctgctgcc cgacaaccac 600  
 tacctgagct accagtccgc cctgagcaaa gaccccaacg agaagcgcgga tcacatggtc 660  
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<210> 4  
 <211> 239  
 <212> PRT  
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 <223> Engineered Aequorea-related fluorescent protein  
 <400> 4

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 1 5 10 15  
 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly  
 20 25 30  
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile  
 35 40 45  
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr  
 50 55 60  
 Phe Gly Tyr Gly Val Gln Cys Phe Ala Arg Tyr Pro Asp His Met Lys  
 65 70 75 80  
 Gln Gln Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu  
 85 90 95  
 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu

100	105	110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly		
115	120	125
Ile Asp Phe Lys Asp Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr		
130	135	140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn		
145	150	155
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser		
165	170	175
Val Gln Pro Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly		
180	185	190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Tyr Gln Ser Ala Leu		
195	200	205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe		
210	215	220
Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys		
225	230	235

<210> 5  
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 S65T, positions 2 to 64  
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Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu		
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Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly		
20	25	30
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35	40	45
Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Phe		
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Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu		
35	40	45
Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys		
50	55	60
Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser		
65	70	75
His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val		
85	90	95
Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala		
100	105	110

Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu  
 115 120 125  
 Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro  
 130 135 140  
 Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala  
 145 150 155 160  
 Gly Ile

<210> 7

<211> 9

<212> PRT

<213> Artificial sequence

<220>

<223> Mutant Green Fluorescent Protein

<400> 7

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<210> 8

<211> 6

<212> PRT

<213> Artificial sequence

<220>

<223> Mutant Green Fluorescent Protein

<400> 8

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<210> 9

<211> 4

<212> PRT

<213> Artificial sequence

<220>

<223> Mutant Green Fluorescent Protein

<400> 9

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<210> 10

<211> 6

<212> PRT

<213> Artificial sequence

<220>

<223> Mutant Green Fluorescent Protein

<400> 10

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<210> 11

<211> 4

<212> PRT

<213> Artificial sequence

<220>

<223> Mutant Green Fluorescent Protein

<400> 11

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1 5

<210> 14  
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Phe Tyr Asn Ile  
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<210> 15  
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<400> 15  
Cys His Gln Arg Trp Tyr Glx  
1 5

<210> 16  
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Phe His Leu Gln Arg Trp Tyr Glx  
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<400> 17

His Lys Asn Gln

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<210> 18

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<220>

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Lys Arg Glu Gly

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<210> 19

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<213> Artificial sequence

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<223> Mutant Green Fluorescent Protein

<400> 19

His Lys Asn Pro Gln Thr

1

5

<210> 20

<211> 5

<212> PRT

<213> Artificial sequence

<220>

<223> Localization sequence targeting the nucleus

<400> 20

Lys Lys Lys Arg Lys

1

5

<210> 21

<211> 26

<212> PRT

<213> Artificial sequence

<220>

<223> Localization sequence targeting mitochondrion

<400> 21

Met Leu Arg Thr Ser Ser Leu Phe Thr Arg Arg Val Gln Pro Ser Leu

1

5

10

15

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Lys Asp Glu Leu

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Met Arg Gly Ser His His His His His His Gly Met Ala Ser Met Thr

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Gly Gly Gln Gln Met Gly Arg Asp Leu Tyr Asp Asp Asp Asp Lys Asp

20                    25                    30

Pro Pro Ala Glu Phe

35